

Claims

1. A method for the detection of a polymorphism in OATP8 in a human which method comprises:
 - (i) determining the sequence of the human at any one of the following positions:
 - 5 positions 743, 811, 2021 and 2380 of SEQ ID NO: 16;
 - positions 233 and 256 of SEQ ID NO: 17; or
 - (ii) determining the sequence of the human, wherein the human is a Caucasian human, at any one of the following positions:
 - 10 positions 389, 410 and 389-392 of SED ID NO: 15;
- 10 positions 378, 1877 and 2501-2505 of SEQ ID NO: 16;
 - position 112 of SEQ ID NO: 17.
2. A method according to claim 1 wherein the polymorphism is further defined as:
 - polymorphism at position 389 is presence of A and/or T;
 - polymorphism at position 410 is presence of T and/or A;
- 15 polymorphism at position 389-392 is presence of ATAT and/or TAGA;
- polymorphism at position 743 is presence of A and/or G;
- polymorphism at position 811 is presence of G and/or C ;
- polymorphism at position 2021 is presence of G and/or A ;
- polymorphism at position 2380 is presence of A and/or T;
- 20 polymorphism at position 378 is presence of G and/or T;
- polymorphism at position 1877 is presence of A and/or G;
- polymorphism at position 2501-2505 is presence of AAAAAA and/or AAAAAAA ;
- polymorphism at position 233 is presence of Ile and/or Met;
- polymorphism at position 256 is presence of Gly and/or Ala; and
- 25 polymorphism at position 112 is presence of Ser and/or Ala.
3. A method according to claim 1 or 2 wherein the method for detection of a nucleic acid polymorphism is selected from amplification refractory mutation system and restriction fragment length polymorphism.
4. Use of a method defined in any of claims 1-3 to assess the pharmacogenetics of a drug transportable by OATP8.
- 30 5. A polynucleotide comprising at least 20 contiguous bases of the human OATP8 gene and comprising an allelic variant selected from any of the following:

Region	variant	Position
Exon 6	G	743 (SEQ ID NO: 16)
Exon 7	C	811 (SEQ ID NO: 16)
Exon 14	A	2021 (SEQ ID NO: 16)
3' UTR	T	2380 (SEQ ID NO: 16)

6. An allele specific primer capable of detecting an OATP8 gene polymorphism at one of the following positions: positions 389, 410 and 389-392 of SEQ ID NO: 15; positions 743, 811, 2021, 2380, 378, 1877 and 2501-2505 of SEQ ID NO: 16.

5 7. An allele specific oligonucleotide probe capable of detecting a OATP8 gene polymorphism at one of the following positions: positions 389, 410 and 289-392 of SEQ ID NO: 15; positions 743, 811, 2021, 2380, 378, 1877 and 2501-2505 of SEQ ID NO: 16.

8. A diagnostic kit comprising an allele specific oligonucleotide probe of claim 7 and/or an allele-specific primer of claim 6.

10 9. A method of treating a human in need of treatment with a drug transportable by OATP8 in which the method comprises detection of a polymorphism in OATP8 in a human, which method comprises:

- (i) determining the sequence of the human at one of the following positions: positions 743, 811, 2021, 2380 of SEQ ID NO: 16;

15 positions 233 and 256 of SEQ ID NO: 17; or

determining the sequence of the human, wherein the human is a Caucasian human, at one of the following positions:

- positions 389,410 and 389-392 of SEQ ID NO: 15;
- positions 378, 1877 and 2501-2505 of SEQ ID NO: 16;

20 position 112 of SEQ ID NO: 17; and

- ii) administering an effective amount of the drug.

10. Use of a drug transportable by OATP8 in preparation of a medicament for treating a disease in a human determined as having a polymorphism at one of the following positions: positions 389, 410 and 389-392 of SEQ ID NO: 15;

25 positions 743, 811, 2021, 2380, 378, 1877 and 2501-2505 of SEQ ID NO: 16;

positions 233, 256 and 112 of SEQ ID NO: 17.

11. An allelic variant of human OATP8 polypeptide comprising:

a methionine at position 233 of SEQ ID NO: 17;

an alanine at position 256 of SEQ ID NO: 17;

an alanine at position 112 of SEQ ID NO: 17;
or a fragment thereof comprising at least 10 amino acids provided that the fragment comprises
the allelic variant at position 233, 256 or 112 of SEQ ID NO: 17.

12. An antibody specific for an allelic variant of human OATP8 polypeptide as described
5 herein having:

a methionine at position 233 of SEQ ID NO: 17;

an alanine at position 256 of SEQ ID NO: 17;

an alanine at position 112 of SEQ ID NO: 17;

or a fragment thereof comprising at least 10 amino acids provided that the fragment comprises
10 the allelic variant at position 233, 256 or 112 of SEQ ID NO: 17.

13. A diagnostic kit comprising an antibody of claim 12.